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COMMUNICATION

A Highly Substituted Pyrazinophane Generated from a Quinoidal System via a Cascade Reaction

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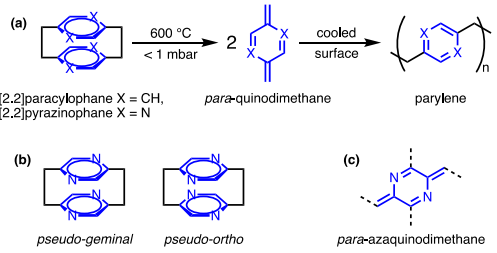
The generation of a highly-substituted [2.2](2,5)pyrazinophane via a cascade reaction is presented. The pyrazinophane product is formed via the dimerization of a member of the para-azaquinodimethane (*p*-AQM) family of conjugated quinoidal compounds—reactivity that sheds light on the nature of stability in *p*-AQMs. Additionally, the electronic and structural nature of this highly-strained ring system are characterized.

Cyclophanes are a class of compounds containing at least one aromatic ring incorporated into a larger macrocycle.[1-9] Perhaps the most well-known and industrially-useful members of this class of compounds are the [2.2]paracyclophanes. [2.2]Paracyclophanes and their derivatives frequently exhibit unique reactivity and electronic properties (Scheme 1a).[4-10] The unique properties of [2.2]paracyclophanes can mostly be attributed to the instability of the strained transannular C-C bonds holding their two rings together, their bent aryl rings, and the intraannular π-electron density exhibited in this family of molecules.[6-11] Many [2.2]paracyclophane derivatives can be thermolyzed in the vapor-phase, yielding substituted *para*-quinodimethane, a compound that spontaneously polymerizes upon condensation to give industrially useful polymers called parylenes (Scheme 1a).[1-8, 13-16] Two isomeric forms of [2.2](2,5)pyrazinophane—a nitrogenous paracyclophane—have also been prepared and polymerized by the above method to yield nitrogen-substituted parylenes (Scheme 1a,b).[2, 7-9, 17] Additionally, [2.2]paracyclophanes have been of recent interest to the organic electronics research community as models of intramolecular charge transfer.[18-21]



Scheme 1 (a) The vapor-phase formation of *para*-quinodimethane and its nitrogenous derivatives from [2.2]paracyclophanes and [2.2]pyrazinophanes, respectively, as well as their spontaneous polymerization to form (substituted) parylenes.[2] (b) the two isomeric forms of [2.2]pyrazinophanes.[7-9] (c) The structure of the *para*-azaquinodimethane motif.[12]

The *p*-AQM family of molecules contain quinoidal nitrogen-substituted rings that are structurally homologous to the *p*-AQM mentioned earlier (Scheme 1c).[12, 17] The synthesis of *p*-AQMs produces compounds with directly conjugated aromatic and quinoidal units, yielding low band-gap organic semiconductors with varied structures. To date, the reported *p*-AQMs have not shown the reactivity that may be expected of such close structural analogs of para-quinodimethane. However, in this communication, we document the spontaneous generation of a novel member of the [2.2(2,5)]pyrazinophane class of molecules from a *p*-AQM derivative and discuss how this reactivity informs our understanding of the reactivity of the *p*-AQM system.

Knoevenagel condensation of thiophene-2-carboxaldehyde with 1,4-diacetyl-2,5-diketopiperazine (**1**) yielded the substituted diketopiperazine **2** (Scheme 2).[12, 17, 22-24] Treatment of **2** with trifluoromethanesulfonic anhydride (Tf_2O) yields the AQM ditriflate, **3** (Scheme 2).[17] Upon subjecting **3** to Stille cross-coupling conditions with 2-tributylstannylthiophene, a yellow compound was isolated along with a significant amount of an intractable gelatinous solid. However, neither of these products are observed if 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) is added to the reaction mixture, indicating that they may be formed via a radical mechanism (See SI).

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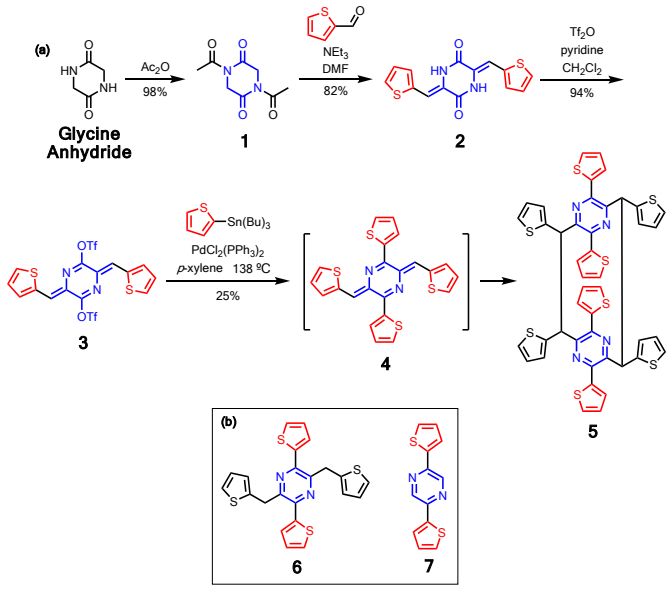

Scheme 2 (a) The synthesis of a [2.2](2,5)pyrazinophane from an activated *p*-AQM intermediate via a cascade reaction. [Ac_2O = acetic anhydride, Tf_2O = trifluoromethanesulfonic anhydride] (b) Structures of monomeric analog **6** and chromophore analog **7**.

Single-crystal X-ray analysis of the yellow compound revealed that while the expected tetrathiophenyl AQM product (**4**) may be formed under the reaction conditions, it is not the isolated product (Figure 1, Scheme 2). Instead, the major soluble product was found to be **5**—a novel member of the small family of [2.2](2,5)pyrazinophanes reported to date (Figure 1, Scheme 2). The reactivity of **4** stands in contrast to other reported dithiophenylidene-AQMs with both electron-withdrawing and donating substituents, for which dimerization has not been observed.[12, 17] Like most [2.2]paracyclophane derivatives, **5** displays two highly bent aromatic rings and an intraannular distance less than what Van der Waals radii would predict (Figure 1). While it is possible in theory to obtain two isomers from this reaction—the *pseudo-ortho* and *pseudo-geminal* geometries—only the former is observed (Scheme 1).[7-9]

The molecular geometry observed in the X-ray structure of **5** displays two notably long (1.59(2) and 1.59(8) Å) transannular carbon-carbon single bonds similar in length to the structures reported for other [2.2]paracyclophanes. As with all *pseudo-ortho* [2.2]pyrazinophanes, **5** is chiral. The dimerization reaction producing **5** simultaneously generates four chiral carbon centers. As revealed by the x-ray structure shown in Figure 1, **5** crystallizes as a racemic mixture, with the (*S,S,S,S*) and (*R,R,R,R*) enantiomers packing in a regular alternating pattern.

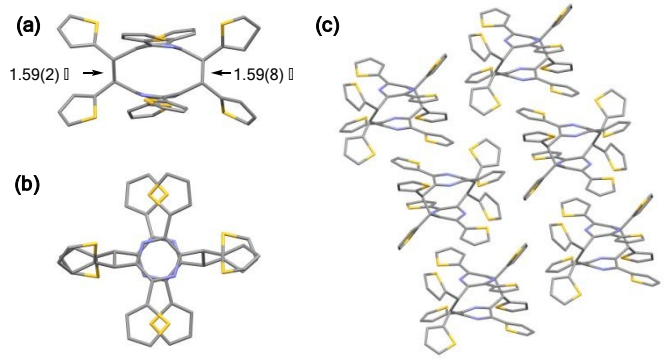

Fig. 1 Stick representation of the single-crystal X-ray structure of **5** showing (a) the side view, with transannular C-C bond lengths indicated, (b) the top view, and (c) molecular packing. H atoms omitted for clarity. C: gray, N: light blue, S: yellow.

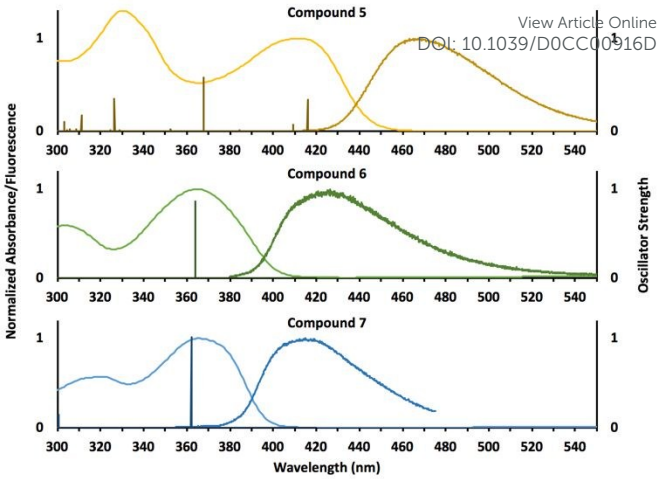

Fig. 2 Normalized UV-visible absorption and fluorescence spectroscopic traces of Compounds **5** (top), **6** (middle), and **7** (bottom) in dichloromethane at 25 °C superimposed upon their respective calculated optical transitions.

The isolation of **5** presented the intriguing opportunity to study the electronic effects of forcing two conjugated ring systems into close proximity. For this reason, two analogs of the expected chromophore (**6** and **7**) were also synthesized and characterized (Scheme 2b, See SI for synthetic details).

UV-Visible absorbance spectroscopy of the AQM pyrazinophane **5** shows a somewhat broad absorbance centered at 411 nm (Figures 2 and S7). This absorbance is bathochromically shifted by 46 nm and 45 nm compared to analogs **6** and **7**, respectively. This shift indicates that there is some effect on the electronics of **5** caused by the close proximity in which its two chromophores are held to each other. A similar effect is seen in fluorescence spectroscopy traces for each compound. Notably, the stokes shifts of compounds **5** and **6** are similar at 57 and 61 nm each, whereas **7** shows a smaller shift of 49 nm. Dimer **5** shows a fairly short fluorescence lifetime (0.43 ns) and a low fluorescence quantum yield (3.66%), indicating that while radiative deexcitation pathways are accessible, nonradiative ones largely outcompete them (Figure S9).

Density Functional Theory (DFT) calculations were undertaken in order to elucidate the electronic distribution in the expected monomeric intermediate (**4**), dimer (**5**), and analog (**6**) and to more fully understand the insights gained from the optical measurements detailed above. Optimized ground-state vacuum geometries and single-point energy levels were determined using the B3LYP functional at the 6-311++G** level for the above-mentioned compounds and the results are summarized in Figures 3, S1, and S2. Additionally, more extensive ground- and excited-state calculations were performed at the PBE0/6-31G* level and the results are shown in Figures S2-S4 and tables S1-S3.

The energy minimized geometries found for **5** closely match the observed single-crystal X-ray structure geometry (Figures 3,

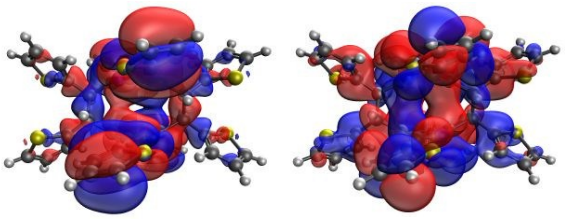

Fig. 3 Frontier molecular orbital density diagrams of **5** calculated at the B3LYP//6-311++G** level, showing intraannular electron density.

S1 and S3). The long transannular C-C bond distances observed in the single-crystal X-ray structure are reproduced computationally, with the geometry-optimized structure of **5** displaying two even transannular C-C bond distances of 1.60 Å. The frontier molecular orbital (FMO) density diagrams of compounds **5**, **6**, and **7** provide more insight about the electronic effects of the pyrazinophane geometry (Figure 3 and S1). The FMO density diagrams of **5** show electron density primarily residing on the dithienylpyrazine chromophores. However, in both of the FMO density diagrams of **5**, significant electron density between the pyrazine rings can be seen, indicating a through-space interaction. The intraannular interaction that this would imply was proposed early on in the study of cyclophanes in order to explain the reduced optical band-gaps of cyclophanes as compared to their monomeric analogs as well as their behavior when reduced or oxidized.[6, 7, 9]

TD-DFT calculations using the TD-PBE0 functional at the 6-31G* level in CH_2Cl_2 on compounds **5**, **6**, and **7** reproduce the optical properties displayed in Figure 3. These calculations allow us to assign the highest-wavelength absorbances of each of the above compounds to $S_0 \rightarrow S_1$ (HOMO→LUMO) transition and to assign the lower-wavelength absorbances (See Table S2).

In an attempt to understand the thermodynamics of the dimerization of **4** to form **5**, the monomeric intermediate **4** was also modelled (PBE0/6-31G* in *p*-xylene). The optimized geometry of **4** was found to deviate significantly from planarity (Figures S1 and S2). A comparison of the total energy of **5** to that of **4** shows that it is thermodynamically favorable (ΔG^0 = -10.35 kcal/mol) for **4** to dimerize. The hypothetical *pseudo*-geminal version of **5** was also investigated computationally, and showed a notably higher total energy than that of the *pseudo*-ortho form. This may help to explain the selectivity for the formation of the *pseudo*-ortho form of **5** (Figure S2).

The unexpected generation of **5** as described above yielded a novel addition to the [2.2]pyrazinophane family of compounds. These compounds are otherwise difficult to access, and routes to generate them may allow for the generation of new functional parylene derivatives. Additionally, the synthesis of **5** showcases the intricacies of stability in the *p*-AQM system—despite the precursor, **3**, in the synthesis of **5** also being a quinoidal *p*-AQM derivative, **3** and many similar compounds were not found to dimerize.[12, 17] This unusual reactivity along with the likelihood of producing unique and useful products warrants further study of the *p*-AQM system.

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Conflicts of interest

There are no conflicts to declare.

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